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Two Cases of COVID-19 Related Cardiomyopathy in Pregnancy.

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1 **Two Cases of COVID-19 Related Cardiomyopathy in Pregnancy.**

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7 The authors report no conflicts of interest.

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12 **Word count:** Abstract 126 words; Manuscript 2112 words

13 **Condensation:** Of seven confirmed COVID-19 infections in pregnant women presenting
14 to a single tertiary care center, two (28.6%) developed cardiomyopathy.

15 **Keywords:** COVID-19, novel coronavirus, pregnancy, cardiomyopathy

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19 **Abstract**

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21 In our institution, 2 of the initial 7 (28.6%; 95% CI 8.2%-64.1%) pregnant patients with
22 confirmed COVID-19 severe infection developed cardiac dysfunction with moderately
23 reduced left ventricular ejection fractions (LVEF) of 40%-45% and hypokinesis. Viral
24 myocarditis and cardiomyopathy have been reported in non-pregnant COVID-19 patients.
25 A case series of non-pregnant COVID-19 patients demonstrated that 33% of those in
26 intensive care developed cardiomyopathy. More data are needed to ascertain the
27 incidence of cardiomyopathy from COVID-19 in pregnancy, in all pregnant COVID-19
28 women, as well as those with severe (e.g. pneumonia) disease. We suggest an
29 echocardiogram in pregnant women with COVID-19 pneumonia, in particular those
30 necessitating oxygen, or critically ill, and we recommend handheld, point-of-care devices
31 where possible to minimize contamination of staff and traditional, large echocardiogram
32 machines.

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43 **Introduction**

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45 Coronavirus 2019 (COVID-19) is a novel coronavirus, responsible currently for a
46 pandemic. The largest cohort to date of over 44,000 individuals from China with
47 COVID-19 infection demonstrated that 81% had mild symptoms up to mild pneumonia,
48 14% had severe disease (dyspnea, hypoxia, or greater than 50% lung involvement on
49 imaging), and 5% had critical disease (respiratory failure, shock, or multiorgan system
50 dysfunction) [1]. It must be noted that in the original report, asymptomatic patients were
51 not tested. Of those with severe disease, the case fatality rate was 49%, while the overall
52 case fatality rate was 2.3% [1]. As most health care systems and countries are only testing
53 symptomatic patients, the true prevalence of COVID-19 infection is unknown, as well as
54 its true infection fatality rate; this has been recently estimated at about 0.66% [2]. Viral
55 myocarditis and cardiomyopathy have been reported in non-pregnant COVID-19 patients
56 [3-4]. A case series of non-pregnant COVID-19 patients in Washington State
57 demonstrated that 33% of those in intensive care developed cardiomyopathy [3].
58 Information on COVID-19 in pregnancy is currently limited [4,5,6]. We are not aware of
59 cardiomyopathy reported in pregnant women with COVID-19 infection. We present 2 of
60 the first 7 pregnant patients with confirmed COVID-19 at a single tertiary care center
61 who presented during March 2020, and developed cardiomyopathy.

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66 **Case Series**

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68 **Case 1:**

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70 A 45 year-old African-American gravida 4 para 2 at 39 weeks and 2 days presented with
71 contractions and emesis on 3/25/2020. The patient had a history of 2 full term vaginal
72 deliveries and was a diet-controlled gestational diabetic (GDMA1). Her BMI was 44.6
73 m²/kg. Her past medical history was significant just for obesity and advanced maternal
74 age. Her only medication was a daily prenatal vitamin. The patient had no known contact
75 with COVID-19 cases and had not traveled outside of the United States in the past month.
76 She was found to be tachycardic with heart rate in the 120s beats/minute, fetal
77 tachycardia with baseline fetal heart rate (FHR) in the 170s beats/minute, and initial
78 temperature of 99.6° F. She was admitted for intravenous fluid hydration and prolonged
79 monitoring. The patient developed a fever of 100.8° F two hours after admission, and
80 work-up revealed a chest radiograph with pulmonary edema and a ground glass
81 appearance. Six hours after presentation she developed severe range hypertension with
82 blood pressure of 183/114 mmHg, HR in the 130s beats/minute, respiratory rate (RR) of
83 26/minute, temperature of 100.7° F and an oxygen saturation (SpO₂) of 96%. Given the
84 severe range blood pressures, a preeclampsia panel was sent which revealed a proteinuria
85 of 1+, platelets of 274,000 per mL, an aspartate aminotransferase (AST) of 32 IU/L and
86 alanine aminotransferase (ALT) of 24 IU/L. A working diagnosis of preeclampsia was
87 established, and magnesium sulfate was initiated for seizure prophylaxis. The patient's

88 RR increased to the 40s/minute and SpO₂ dropped to 80% on oxygen via nasal cannula.
89 After a discussion with maternal-fetal medicine, anesthesia, general obstetrics and
90 gynecology, and cardiology, the decision was made to deliver the fetus to aid maternal
91 resuscitation. The patient underwent a primary cesarean delivery 7.5 hours after
92 presentation on 3/26/2020. On postoperative day (POD) #0 a maternal arterial blood gas
93 (ABG) showed pH of 7.27, pCO₂ of 31 mmHg, pO₂ of 117 mmHg, HCO₃ of 16 mEq/L,
94 and a base excess of -11 mmol/L. A repeat chest radiograph revealed small peripheral
95 bilateral opacities with differential diagnoses including atypical pneumonia, viral
96 pneumonia, and congestive heart failure. Due to suspicion of congestive heart failure,
97 magnesium sulfate was discontinued and furosemide was administered IV. Cardiology
98 was consulted to perform an echocardiogram, which showed a moderately reduced left
99 ventricular ejection fraction (LVEF) of 40% with global hypokinesis, and she was
100 diagnosed with acute heart failure with reduced EF. Given the clinical picture of fever,
101 tachypnea, and the chest radiograph findings amidst the background of a pandemic, a
102 GeneXpert COVID-19 RNA polymerase chain reaction (PCR) test was performed and
103 returned positive. Further laboratory investigation demonstrated a normal troponin of
104 0.046 ng/mL, a brain natriuretic peptide (BNP) of 114 pg/mL (normal <100 pg/mL), and
105 a procalcitonin of 0.13 ng/mL (normal < 0.10 ng/mL). On POD #4, chest radiograph
106 demonstrated worsening bilateral lung infiltrates, and despite oxygen therapy, the SpO₂
107 could not be maintained above 90%. An electrocardiogram was performed with non-
108 specific T-wave abnormalities otherwise a normal EKG, with a QT/QTc of 354/465 ms
109 (both normal). Serum potassium was 3.7 mEq/L (normal). As the patient failed to
110 improve, she was started on methylprednisolone IV 60mg every 3 hours and

111 hydroxychloroquine 400mg orally every 12 hours for 24 hours, followed by 400mg orally
112 daily. That evening, after the initial doses were administered, she began desaturating to
113 86% on 6 liters of nasal cannula. An ABG revealed a pH of 7.07, pCO₂ of 75 mmHg,
114 pO₂ of 85 mmHg, HCO₃ of 21.7 mEq/L, and a BE of -2 mmol/L. She was placed on a
115 non-rebreather at 15 liters, which initially improved the SpO₂ to 90% and on POD #4
116 methylprednisolone 100mg IV daily was started. On POD #5 the patient again
117 desaturated to the low 80's%. As our institutional COVID-19 protocol calls to avoid non-
118 invasive mechanical ventilation which could aerosolize viral particles, the patient was
119 intubated by anesthesia, but without improvement. The heart rate decreased to the 30's
120 and the patient developed pulseless electrical activity (PEA). Cardiopulmonary
121 resuscitation (CPR) was initiated and return of spontaneous circulation (ROSC) was
122 obtained after 5 minutes of CPR. Post arrest her troponin level peaked at 0.930 ng/mL
123 (normal <0.4 ng/mL), with a BNP of 323 pg/mL. After CPR the patient was started on a
124 norepinephrine drip, initially at 8 mcg/minute and was titrated up to a maximum of 20
125 mcg/min. The patient was administered one dose of Tocilizumab, an interleukin-6 (IL-6)
126 receptor antagonist 800mg IV. As of the writing of this article (4/2/2020), the patient is
127 currently POD #7 and remains intubated and ventilated in the ICU, is arousable and
128 moving all four extremities, with an SpO₂ of 96%, continuance of the norepinephrine
129 drip at 20 mcg/min, daily methylprednisolone 100mg IV daily, and hydroxychloroquine
130 400mg PO daily. Her significant laboratory values are: troponin 0.046 ng/mL and a
131 markedly elevated procalcitonin of 48.21ng/mL.

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133 **Case 2:**

134 A 26 year-old Latin American gravida 3 para 1 at 33 weeks and 6 days presented with
135 shortness of breath, dyspnea, and decreased fetal movement on 3/27/2020. The patient
136 has a history of 1 full-term vaginal delivery and the patient's husband was known to be
137 positive with COVID-19 infection. Her BMI was 37 m²/kg. Her past medical history was
138 significant also for polycystic ovary syndrome, and her only medication was a daily
139 prenatal vitamin. The patient's initial vital signs were HR in the 130s beats/minute, BP of
140 110s/70s mmHg, RR in the mid-20's/minute, an SpO₂ of 95%, and an initial temperature
141 of 99.3° F. The SpO₂ improved to 97% on 2L nasal cannula. About 8 hours after
142 presentation, her RR increased to the 40s/minute, with a HR in the 130s/minute, and
143 SpO₂ of 95%. An ABG showed a pH of 7.32, pCO₂ of 18 mmHg, pO₂ of 107 mmHg,
144 HCO₃ of 14 mEq/L, and a BE of -14 mmol/L. CXR demonstrated bilateral infiltrates.
145 Work-up for metabolic acidosis with respiratory alkalosis was significant for an anion
146 gap of 19, which when investigated, only demonstrated an elevated beta-hydroxybutyrate
147 of 3.61 mmol/L (normal 0.02 to 0.27 mmol/L). Lactic acid was 0.6 mmol/L (normal 0.4
148 to 2.0 mmol/L) and the other differential diagnoses for anion gap acidosis were ruled out.
149 As there was suspicion for COVID-19 infection, a general respiratory panel was sent and
150 was negative, C-Reactive Protein (non cardiac) was 7.68 mg/dL (normal <3.0 mg/L),
151 ferritin of 86 ng/mL, BNP of <10 pg/mL, procalcitonin of 0.17 ng/mL, troponin-I of
152 <0.015, AST of 47 IU/L, and an ALT of 52 IU/L. Becton Dickinson COVID-19 testing,
153 which was sent on 3/28/2020, returned positive. The patient was managed with fluid
154 restriction, supplemental oxygen via nasal cannula, ceftriaxone IV and azithromycin IV.
155 Given our contemporary experience with the patient presented in Case #1, out of
156 precaution an echocardiogram was performed that demonstrated a moderately reduced

157 LVEF of 40-45% with global hypokinesis. Her SpO₂ was 96% on room air. Despite her
158 reduced EF, cardiology did not feel she was clinically in acute heart failure; metoprolol
159 12.5mg twice a day was initiated and the patient was placed on a telemetry monitoring.
160 Her HR was in the 100s, BP of 110s/70s, RR of 20s, with ABG showing a pH of 7.42,
161 pCO₂ of 28.7 mmHg, pO₂ of 101 mmHg, HCO₃ of 18.8 mEq/L, and a BE of -6 mmol/L.
162 Given the unknown course of COVID-19 in pregnancy, as a precaution, and in an effort
163 to deliver the patient before becoming critically ill, the patient underwent a primary
164 cesarean delivery on 4/1/2020 and was recovered with continuous telemetry monitoring.
165 As of the writing of this article (4/2/2020) the patient is currently stable on day #7 of
166 hospital admission and POD #1 from cesarean delivery. She is meeting her POD #1
167 surgical goals, with an improved respiratory status and SpO₂ of 96% on room air.
168 However, overnight the patient developed supraventricular tachycardia (SVT), therefore,
169 cardiology increased her metoprolol from 12.5mg PO q12 to 25mg PO q12. Of note,
170 during her entire hospitalization, the patient never developed a fever >100.4° F. As per
171 Center for Disease Control, both the mother and neonate are being isolated from the
172 general postpartum population in negative pressure rooms with droplet isolation.

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175 **Discussion:**

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177 A review of the literature demonstrates that cardiomyopathy is a frequent finding in up to
178 33% of critically ill, non-pregnant COVID-19 patients [3,4]. It is unknown if the rate of
179 developing COVID-19 cardiomyopathy is exacerbated in the pregnant population or

180 similar to the rate in the non-pregnant patient. Additionally, it is unclear whether the high
181 rate of cardiomyopathy reported in the case series of non-pregnant patients is secondary
182 to multisystem organ dysfunction or a direct complication of COVID-19. It must be
183 highlighted that our cohort of COVID-19 positive pregnant women is currently limited,
184 and that we are only testing symptomatic pregnant patients; the association between
185 cardiomyopathy and COVID-19 infection in pregnancy is possibly less strong than what
186 we found. Our two patients had some risk factors for cardiac disease, including
187 race/ethnic group, obesity, and in one case advanced maternal age.

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189 Pregnancy is an immunocompromised state in which the cardiovascular demands are
190 increased. It is a state of compensated respiratory alkalosis with metabolic acidosis that is
191 vulnerable to respiratory pathogens such as COVID-19. Of the respiratory parameters,
192 respiratory rate remains unchanged in healthy pregnancy, and the finding of tachypnea is
193 a significant finding and should prompt practitioners to further evaluate the patient.
194 While tachypnea and shortness of breath are not unique findings to COVID-19 infection
195 or cardiomyopathy, in the critically ill COVID-19 pregnant woman, or even in the
196 pregnant woman with COVID-19 pneumonia necessitating oxygen, given also the
197 evidence from the non-pregnant literature, performing an echocardiogram should be
198 considered to evaluate for cardiomyopathy. Furthermore, to minimize exposure to
199 echocardiographer technologists and to avoid contamination of the traditional
200 echocardiogram machines that could serve as a fomite and infect the next patient, a
201 policy whereby board certified echocardiography cardiologists perform the study with,
202 for example, a point-of-care handheld General Electric Vscan echocardiography device is

203 suggested. This small device is easy to decontaminate, is of good technical quality and
204 images are stored, downloaded into the patient's electronic medical record and
205 interpreted into a formal report. The management, evaluation, and ability to anticipate
206 complications in pregnant patients are critical in this COVID-19 pandemic; more
207 experience is needed.

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227

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